
Deaths from Gallstones

Incidence and Associated Clinical Factors

GIOVANNI CUCCHIARO, M.D., CHRISTOPHER R. WATTERS, M.D., JOHN C. ROSSITCH, M.D.,
and WILLIAM C. MEYERS, M.D.,

The purpose of this study was to determine the incidence of death as the initial manifestation of cholelithiasis. Records of patients who died or underwent cholecystectomy for gallstone-related disease at Duke University Medical Center between 1976 and 1985 were reviewed. Thirty patients died, six of whom (20%) had previous episodes of biliary pain and stone documentation. Twenty-four (80%) were asymptomatic (three with previous incidental diagnosis of cholelithiasis). Reason for admission included acute cholecystitis (nine), pancreatitis (eight), biliary pain (six), cholangitis (four), jaundice (one), and endocarditis (one). Three patients died of gallstone complications without surgical intervention; one patient had renal failure and two had septicemia. Other causes of death were: sepsis (seven patients), cardiac failure (six), pulmonary complications (four), renal failure (three), cerebrovascular accident (three), liver failure (two), pancreatitis (one), and gastrointestinal bleeding (one). During this period, 1731 cholecystectomies were performed without mortality. In this group, the patients were younger (50 ± 8 years vs. 64 ± 13 years, $p < 0.001$), and had a lower incidence of cirrhosis ($p < 0.001$) and diabetes ($p < 0.002$). The sex ratio was inverted ($p < 0.001$). This study demonstrates that death from gallstones is uncommon (three cases per year), as is death from their initial clinical manifestation (1.2%). The risk of death is two- and ninefold higher in patients with acute cholecystitis or acute pancreatitis. Age, cirrhosis, and diabetes are important determinants of outcome.

RECENT STUDIES indicate that the prevalence of gallstones ranges from 5% to 44%, depending on the patient population.¹⁻⁴ The incidence of symptoms in patients with cholelithiasis is between 9% and 37%.^{5,6,8} Less than half of symptomatic patients undergo biliary tract operations. The probability of an asymptomatic patient developing biliary pain is 10-31%,^{8,9} and only 7% eventually have surgery.⁸ These data do not support prophylactic cholecystectomy or any other treatment for silent gallstones, if one assumes that

From the Department of Surgery, Duke University Medical Center, Durham, North Carolina

one can wait without risk of the development of symptoms. Data on the incidence of death or life-threatening complication as the initial manifestation of cholelithiasis are not available. Several studies have discussed the influence of associated diseases on morbidity and mortality in patients with cholelithiasis. The purpose of this study is to evaluate the prevalence of death resulting from the initial complication of gallstones and to determine the causes of those deaths.

Methods

We reviewed the medical and pathologic records of patients who died between 1976 and 1985 at Duke University Medical Center with gallstone disease diagnosed within the first 24 hours of admission as the primary problem. The review included analyses of age, sex, previous biliary symptoms, nonbiliary diseases, acute complications, and management of the cholelithiasis. Deaths were considered gallstone-related when cholelithiasis and its complications were determined by clinical diagnosis or autopsy to be responsible for death. Excluded from the analysis were patients who had gallbladder cancer, acalculous cholecystitis, or calculous cholecystitis that developed during hospitalization after the first 24 hours. These patients were subsequently compared with patients who underwent successful cholecystectomy at this hospital during the same period. Statistical analysis for continuous variables was performed using Student's *t*-test for unpaired data and chi-square for categorical variables.¹⁰

Results

Thirty patients died at Duke University Medical Center as a direct consequence of gallstone disease during this

Reprints requests and correspondence: W.C. Meyers, M.D., Department of Surgery, PO Box 3041, Duke University Medical Center, Durham, NC 27710.

Submitted for Publication: June 16, 1988.

TABLE 1. *Complications of Gallstone Disease*

| Complications | No. of Patients |
|---------------------|-----------------|
| Acute cholecystitis | 9 |
| Pancreatitis | 8 |
| Biliary pain | 6 |
| Cholangitis | 4 |
| Icterus | 1 |
| Endocarditis | 1 |

10-year period. The mean age of these patients was 64 ± 13 years (range of 39–89 years). Eighteen of the patients were men, and twelve were women. Nineteen patients were transferred to Duke University Medical Center for the management of complications resulting from cholelithiasis; all of the nineteen patients initially required intensive care units for management. Six patients (20%) had previous episodes of biliary pain and documentation of stones in the gallbladder, but none had undergone cholecystectomy. These six patients were admitted an average of 4.8 months after the diagnosis of cholelithiasis. All but one underwent an emergency operation. Twenty-four patients (80%) were previously asymptomatic. Three of these patients (10%) had documented gallstones; one had undergone elective cholecystectomy, one underwent an emergency cholecystectomy, and one died of septic complications of cholelithiasis without surgical intervention. The other 21 asymptomatic patients (70%) had no previously documented gallstone; all but two underwent emergency operation. Two patients never underwent surgery and died of renal or septic complications of cholelithiasis. The gallstone complications observed at admission are listed in Table 1. Acute cholecystitis, pancreatitis, and cholangitis were the most frequent complications. The most common associated, nonbiliary diseases were diabetes (seven patients), cardiovascular disease, including previous myocardial infarction, coronary artery diseases, cardiac arrhythmias, heart failure, and valve disease (six), cirrhosis (four), and chronic pulmonary disease (two). One patient had lymphoma and another had morbid obesity. The causes of death are listed in Table 2. In twenty-six patients, the clinical impression was confirmed by autopsy. The majority of deaths were due to sepsis or cardiopulmonary failure.

TABLE 2. *Cause of Death*

| Cause of Death | No. of Patients |
|---------------------------|-----------------|
| Sepsis | 9 |
| Cardiac failure | 6 |
| Pulmonary complications | 4 |
| Renal failure | 4 |
| Cerebrovascular accident | 3 |
| Liver failure | 2 |
| Gastrointestinal bleeding | 1 |
| Pancreatitis | 1 |

CHOLECYSTECTOMIES FOR CHOLELITHIASIS

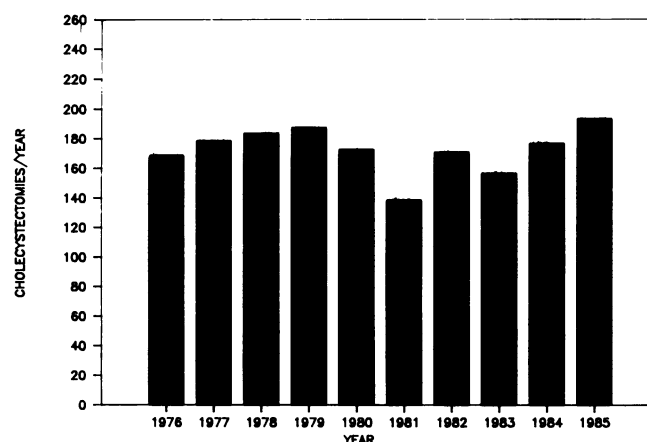


FIG. 1. Numbers of cholecystectomies for cholelithiasis at Duke University Medical Center in 10 years period.

During the same 10-year period, 1731 cholecystectomies were performed for cholelithiasis. The annual rate was 173 (range of 139–188) (Fig. 1). The mean age of these patients was 50 ± 8.2 years, which is significantly lower than in the nonsurvivors group ($p < 0.001$). One thousand two hundred nine were women, and 522 were men. The sex ratio was statistically different than for the patients who died ($p < 0.001$). The most frequent complications of gallstone disease in the survivor group were acute cholecystitis (245 patients), and acute pancreatitis (51 patients). Acute cholecystitis and acute pancreatitis occurred significantly more frequently in patients who died (30% vs. 14%, and 27% vs. 3%: $p < 0.02$ and $p < 0.001$, respectively). Age, diabetes, and cirrhosis were other significant risk factors (Table 3).

Discussion

From these data, it is clear that death from gallstone disease is an uncommon event (three cases per year at this medical center). In this series, the overall operative mortality for elective and emergency surgery was 1.5%, which is consistent with earlier series.¹¹⁻¹⁴ In 21 patients,

TABLE 3. *Risk Factors of the Study Population*

| Risk Factors | Alive (n = 1731) | Dead (n = 30) | p value |
|------------------------|---------------------|------------------|---------|
| Sex (M/F) | 522/1209 | 18/12 | 0.001 |
| Age | 50.0 ± 8.2 | 64.0 ± 13.4 | 0.001 |
| Liver cirrhosis | 23 | 4 | 0.001 |
| Diabetes | 137 | 7 | 0.002 |
| Cardiovascular disease | 168 | 6 | NS |
| Obesity | 101 | 1 | NS |
| Pulmonary diseases | 45 | 2 | NS |
| Renal diseases | 6 | 0 | NS |

the initial complication of gallstone disease proved lethal. With regard to factors that influenced the mortality in our population, we could identify several risk factors. Elderly patients were more likely to die, and this is not surprising because they had more frequent medical problems. Sex also seems to play a role, as evidenced by the inverted sex ratios between survivors and nonsurvivors. However, we cannot explain why the men were at greater risk of dying. It is possible that men with gallstones also have more associated risk factors. Some suggestion for this possibility is provided in the recent paper of Sandler et al.¹⁶ In that study, too, men were at greater risk of having complications, as a consequence of concomitant disease, compared with women. Patients who developed acute cholecystitis or acute pancreatitis were two and nine times as likely to die, respectively. With regard to associated diseases, cirrhosis and diabetes occurred significantly more frequently in the nonsurvivor group.

Numerous recent studies have examined the prevalence and natural history of gallstone disease in Europe and in the United States.⁸⁻¹⁵ These showed that cholelithiasis is a common disease, but also that it becomes symptomatic in only 9–37% of cases. Therefore, the natural history of asymptomatic patients would seem to be benign if the probability of dying at the time of initial manifestation of cholelithiasis is very low. The present observations indicate a low likelihood for developing life-threatening complications as an initial manifestation of cholelithiasis (1.2%). On that basis of these data, we do not generally recommend prophylactic cholecystectomy in asymptomatic gallstone patients. Liver cirrhosis and diabetes were important determinants of fatal outcome in asymptomatic patients. Should a cirrhotic patient with silent gallstones have prophylactic cholecystectomy? The answer is probably no,¹⁷ considering that these patients are at increased risk even for elective surgery, although in selected patients with well-compensated cirrhosis and symptomatic stones, cholecystectomy may be advised.¹⁸⁻¹⁹ With respect to diabetes, our results do not support the recently published observations¹⁶⁻²⁰ that diabetes *per se* does not influence the risk of life-threatening complications of cholelithiasis. Although diabetes is not responsible for an increased risk, cardiovascular, renal, and vascular occlusive disease associated with diabetes are important risk factors. In addition, diabetics with gallstones are not at increased risk for elective surgery.²⁰⁻²² Our data indeed show that severe complications of cholelithiasis are more common among diabetic patients, lending support to the empiric recommendation of early prophylactic cholecystectomy in these patients.

Acknowledgments

The authors are grateful to Mary Ann Branum and Karen H. Hollingsworth for their clinical research assistance, and to Carolyn F. Greene for preparation of this manuscript.

References

- Galvao H, Menezes ML, Correia JP. The prevalence of gallstones in the Portuguese population. A necropsy study. *Ital J Gastroenterol* 1981; 13:100–104.
- Lindstrom CG. Frequency of gallstone disease in a well-defined Swedish population. *Scand J Gastroenterol* 1977; 12:341–346.
- Glenn F. Biliary tract disease. *Surg Gynecol Obstet* 1981; 153:401–402.
- Balzer K, Goebell H, Breuer N, et al. Epidemiology of gallstones in a German industrial town (Essen) from 1940–1975. *Digestion* 1986; 33:189–197.
- Rome group for the epidemiology and prediction of cholelithiasis (GREPCO). Prevalence of gallstone disease in an Italian adult female population. *Am J Epidemiol* 1984; 119:706–805.
- Godfrey PJ, Bates T, Harrison M, et al. Gallstones and mortality: a study of all gallstone-related deaths in a single health district. *Gut* 1984; 25:1029–1033.
- Gracie WA, Ransohoff DF. The natural history of silent gallstones. *New Engl J Med* 1982; 307:798–800.
- Thistle JL, Cleary PA, Lachin JM, et al. Steering Committee National Cooperative Gallstone Study Group. The natural history of cholelithiasis. *Ann Int Med* 1984; 101:171–175.
- McSherry CK, Ferstenberg H, Calnoun WF, et al. The natural history of diagnosed gallstone disease in symptomatic and asymptomatic patients. *Ann Surg* 1985; 202:60–63.
- Schwartz D., *Methods Statistiques*. Paris: Flammarion Medicine Sciences, 1986; 141–166.
- Commission on Professional and Hospital Activities. Hospital Mortality, PAS Hospitals, United States 1974–1975. Ann Arbor, Michigan, 1977; Table F.
- Bishop YMM, Mosteller F. Smoothed contingency-table analysis. In JP Bunker, WH Forrest Jr, F Mosteller, LD Vandam, eds. *The National Halothane Study*. Bethesda: National Institute of General Medical Sciences, 1969; 238–272.
- Meyer KA, Capos NJ, Mittelpunk AI. Personal experiences with 1261 cases of acute and chronic cholecystitis and cholelithiasis. *Surgery* 1967; 61:661–668.
- Chigot JP. Le risque operative dans la lithiase biliaire: a propos de 5433 interventions. *Semin Hop Paris* 1981; 57:1311–1319.
- Barker DJP, Gardner MJ, Power C, Hutt MSR. Prevalence of gallstones at necropsy in nine British towns: a collaborative study. *Br Med J* 1979; 2:1389–1392.
- Sandler RS, Maule WF, Baltus ME. Factors associated with post-operative complications in diabetes after biliary tract surgery. *Gastroenterology* 1986; 91:157–162.
- Aranha GV, Sontag SJ, Greenber HB. Cholecystectomy in cirrhotic patients: a formidable operation. *Am J Surgery* 1982; 143:55–60.
- Bloch RS, Allaban RD, Walt AJ. Cholecystectomy in patients with cirrhosis: a surgical challenge. *Arch Surg* 1985; 120:669–672.
- Castaing D, Houssin D, Lemoine J. Surgical management of gallstones in cirrhotic patients. *Am J Surg* 1983; 146:310–313.
- Walsh DB, Eckauser FE, Ramsburg SR, Burney RB. Risk associated with diabetes mellitus in patients undergoing gallbladder surgery. *Surgery* 1982; 91:254–257.
- Hjortrup A, Sorensen C, Dyremose E, et al. Influence of diabetes mellitus on operative risk. *Br J Surg* 1985; 72:783–785.
- Reiss R, Deutsch AA, Nudelmann J. Biliary surgery in diabetic patients: statistical analysis of 189 patients. *Dig Surg* 1987; 4:37–40.